REMARKS

Claims 1 and 3-18 are pending and claims 19-40 are withdrawn as directed to a non-elected species. Claim 2 is cancelled herein without prejudice. Claim 1 is amended to recite mulitpotent neural stem cells derived from neural tissue, support for which can be found at least at page 7, lines 4-9.

Improper Finality of Office Action

The Applicant objectd to the finality of the Office Action of May 18, 2007. MPEP § 706.07(a) states that "[u]nder present practice, second or any subsequent actions on the merits shall be final, except where the examiner introduces a new ground of rejection that is neither necessitated by applicant's amendment of the claims nor based on information submitted in an information disclosure statement . . . ." The Office Action of May 18, 2007 introduces, *for the first time*, a rejection under 35 U.S.C. § 112. The Applicant's previous amendment included no claim amendments and the rejection under 35 U.S.C. §112 is, by definition, not a prior art rejection. Thus, a new ground of rejection has been introduced that was neither necessitated by amendments to the claims nor based on information submitted in an IDS.

For these reasons, the Applicant requests that the finality of the Office Action of May 18, 2007, be withdrawn.

35 U.S.C. § 112

Claims 1-4 and 10-18 are rejected under 35 U.S.C. §112, first paragraph, for allegedly not enabling "a method of producing oligodendrocytes from all types of neural stem cells isolated from any mammal at any developmental stage while the cells are located in a mammal (i.e., *in vivo*)." Specifically, the Examiner alleges that undue experimentation would be required to perform the *in vivo* aspect of the pending claims.

The Applicant provides herewith a Declaration Under 37 C.F.R. § 1.132 by Samuel Weiss ("Weiss Declaration") providing experimental evidence showing that the methods taught herein are enabled. The data show that GM-CSF promotes the proliferation and survival of

oligodendrocytes *in vivo*. Specifically, GM-CSF was infused into 6-week old CD1 male mice for 6 days followed by examination of the factor's effects in the corpus callosum. Immunohistochemistry with antibodies against PDGFRα and GSTπ (*see* Figure 1, Weiss Declaration) was used to quantify the number of oligodendrocyte progenitor cells and the total number of mature oligodendrocytes in the corpus callosum. GM-CSF increased the number of BrdU-positive cells in the corpus callosum by 17-fold ($p < 0.001$; $n = 5$) (*see* Table 1, Weiss Declaration). Further, GM-CSF increased the number of newly generated PDGFRα/BrdU-positive cells by 23-fold ($p < 0.001$; $n = 5$) (*see* Table 1, Figures 1 and 2, Weiss Declaration). GM-CSF also increased the percentage of PDGFRα/BrdU-positive cells of the total PDGFRα-positive cells compared to control infusions by a similar factor (*see* Table 1, Weiss Declaration). These results indicate that GM-CSF increases production of new oligodendrocytes. When examining the number of terminally differentiated oligodendrocytes in the corpus callosum, GM-CSF increased the number of GSTπ-positive cells by approximately 2-fold compared to control (*see* Table 1, Weiss Declaration), and resulted in a significantly greater number of GSTπ/BrdU-positive cells (*see* Figure 2, Weiss Declaration). This number of GSTπ/BrdU-positive cells was approximately 7-fold as compared to the control level ($p < 0.01$; $n = 5$) (*see* Figure 1, Weiss Declaration). GM-CSF also significantly increased the percent of GSTπ/BrdU-positive cells of the total number of GSTπ-positive cells by approximately 4-fold as compared to the control level ($p < 0.01$; $n = 5$) (*see* Table 1, Weiss Declaration). These results indicate that GM-CSF increases the number of terminally differentiated oligodendrocytes in the corpus callosum.

Further, the number of apoptotic terminally differentiated oligodendrocytes in the corpus callosum following ICV infusion of GM-CSF was examined by immunostaining for the activated form of caspace-3, a marker of apoptotic cells, and GSTπ (*see* Figures 1 and 2, Weiss Declaration). There were significantly fewer activated caspase-3-positive cells in the corpus callosum following GM-CSF infusion compared to control ($p < 0.05$; $n = 4$ for GM-CSF animals, $n = 5$ for control animals) (*see* Table 1, Weiss Declaration). When examining the number of apoptotic oligodendrocytes, there were significantly fewer activated caspase-3/GSTp-positive cells following GM-CSF infusion compared to control infusions ($p < 0.05$; $n = 4$ for GM-CSF animals, $n = 5$ for control animals) (*see* Table 1 and Figure 1, Weiss Declaration).

These data indicatet that GM-CSF promoted the survival of terminally differentiated oligodendrocytes *in vivo* in the corpus callosum.

Contrary to the Examiner's position that *in vivo* use is not enabled, these data show that GM-CSF enhances the survival of mature oligodendrocytes *in vivo*. Further, these data demonstrate that one of skill in the art could practice the method commensurate in scope with the claims without undue experimentation.

As noted by the Examiner, the test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art without undue experimentation. Further, the MPEP notes at 2164.08 that "[a]ll that is necessary is that one skilled in the art be able to practice the claimed invention, given the level of knowledge and skill in the art." Contrary to the Examiner's position that *in vivo* use is not enabled, the data discussed above show that the methods taught and claimed enable one of skill in the art to enhance the survival of mature oligodendrocytes *in vivo*. One of skill in the art could practice the invention commensurate in scope with the claims without undue experimentation. The existence of references that note the difficulty of developing and performing such methods is completely irrelevant when experimental data, such as that discussed above, is provided to demonstrate that one of skill in the art could perform the disclosed methods. Because the present specification enables the claimed methods, the Applicant requests that the rejection of claims 1-4 and 10-18 under 35 U.S.C. § 112 be withdrawn.

35 U.S.C. § 102—Mehler

Claims 1, 2, 6-9, 12, 14, 15, 17, and 28 are rejected under 35 U.S.C. § 102(b) as being anticipated by Mehler et al., Int. J. Devl. Neuroscience 13:213-240 (1995) ("Mehler"). Claim 2 is cancelled herein, thereby rendering the rejection as to that claim moot.

As amended, claim 1 recites contacting multipotent neural stem cells with an effective amount of at least one oligodendrocyte promoting factor under conditions that result in production of oligodendrocytes from the multipotent neural stem cells, wherein the oligodendrocyte promoting factor is selected from the group consisting of granulocyte-macrophage colony stimulating factor (GM-CSF), interleukin 3 (IL-3) and interleukin 5 (IL-5).

The cited portions of Mehler do not disclose contacting multipotent neural stem cells with an effective amount of at least one oligodendrocyte promoting factor under conditions that result in production of oligodendrocytes from the multipotent neural stem cells, wherein the oligodendrocyte promoting factor is selected from the group consisting of granulocyte-macrophage colony stimulating factor (GM-CSF), interleukin 3 (IL-3) and interleukin 5 (IL-5). Because Mehler does not disclose or suggest providing GM-CSF, IL-3, or IL-5 under conditions that result in production of oligodendrocytes from multipotent neural stem cells, amended claim 1 cannot be anticipated by Mehler under 35 U.S.C. § 102(b). Claims 6-9, 12, 14, 15, 17, and 18 depend from claim 1 and include all the limitations of claim 1. Thus, claims 6-9, 12, 14, 15, 17, and 18 also are not anticipated by Mehler under 35 U.S.C. § 102(b), and the Applicant requests that the rejection as to all claims be withdrawn.

35 U.S.C. § 102—Tennekoon

Claims 1, 2, 5, 12-15, 17, and 18 are rejected under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No. 6,673,606 to Tennekoon et al. ("Tennekoon").

As amended, claim 1 recites contacting multipotent neural stem cells with an effective amount of at least one oligodendrocyte promoting factor under conditions that result in production of oligodendrocytes from the multipotent neural stem cells, wherein the oligodendrocyte promoting factor is selected from the group consisting of granulocyte-macrophage colony stimulating factor (GM-CSF), interleukin 3 (IL-3) and interleukin 5 (IL-5). Tennekoon does not disclose contacting multipotent neural stem cells with an effective amount of at least one oligodendrocyte promoting factor under conditions that result in production of oligodendrocytes from the multipotent neural stem cells, wherein the oligodendrocyte promoting factor is selected from the group consisting of granulocyte-macrophage colony stimulating factor (GM-CSF), interleukin 3 (IL-3) and interleukin 5 (IL-5).

Although the Applicant believes the multipotent neural stem cells used in the present methods are distinguishable from mesenchymal stromal cells, claim 1 has been amended to facilitate prosecution. Specifically, claim 1 is amended to recite that the multipotent neural stem cells are derived from neural tissue. The mesenchymal stem cells of Tennekoon are isolated

from bone marrow and not neural tissue. Therefore, Tennekoon fails to teach each element of claim 1 and cannot anticipate claim 1.

Because Tennekoon does not disclose or suggest contacting multipotent neural stem cells with an effective amount of at least one oligodendrocyte promoting factor under conditions that result in production of oligodendrocytes from the multipotent neural stem cells derived from neural tissue, wherein the oligodendrocyte promoting factor is selected from the group consisting of granulocyte-macrophage colony stimulating factor (GM-CSF), interleukin 3 (IL-3) and interleukin 5 (IL-5), amended claim 1 cannot be anticipated by Tennekoon under 35 U.S.C. § 102(b) and the Applicant requests that the rejection be withdrawn. Claims 2, 5, 12-15, 17, and 18 depend from claim 1 and recite limitations that further differentiate the claims from Tennekoon; thus, these claims also cannot be anticipated by Tennekoon under 35 U.S.C. § 102(b). The Applicant requests that the rejection be withdrawn.

35 U.S.C. § 103 Tennekoon *et al.* and Magil *et al.*

Claim 16 is rejected as being unpatentable under 35 U.S.C. § 103(a) over Tennekoon in view of U.S. Patent Publication No. 2003/0171269 by Magil et al., ("Magil").

As discussed above, Tennekoon's mesenchymal stromal cells are not neural stem cells derived from neural tissue. Magil does not make up for this deficiency in Tennekoon. Additionally, Tennekoon's indication that neural stem cells have drawbacks and are difficult to obtain (see column 1, lines 56-63) teaches away from using neural stem cells. For these reasons, claim 16 is patentable over Tennekoon in view of Magil, and the Applicant requests the withdrawal of this rejection.

Conclusions

For the reasons set forth above, the Applicant submits that the claims of this application are allowable. Reconsideration and withdrawal of the Examiner's rejections are hereby requested. Allowance of the claims remaining in this application is earnestly solicited. At a minimum, the Applicant requests entry of the Amendment so that the application is in condition for appeal.

In the event that a telephone conversation could expedite the prosecution of this application, the Examiner is requested to call the undersigned at 404-892-5005.

No fees are believed to be due with this Amendment, however, please apply any charges or credits to deposit account 06-1050.

Respectfully submitted,

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